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09/929,328	08/13/2001	Ilya Raskin	29155/37272	8759

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EXAMINER	
AFREMOVA, VERA	
ART UNIT	PAPER NUMBER
1651	9

DATE MAILED: 07/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/929,328	Raskin et al.
Examiner	**Art Unit**
Vera Afremova	1651

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 6, 2003*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4 and 6-26* plication.

4a) Of the above, claim(s) consideration.

5) ☐ Claim(s)

6) ☒ Claim(s) *1-4 and 6-26*

7) ☐ Claim(s)

8) ☐ Claims are subject to restriction and/or election requirement.

file

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).
4) ☐ Interview Summary (PTO-413) Paper No(s).
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of claims

Claims 1-4 and 6-26 as amended are pending and under examination. [Paper No. 8 filed 5/06/2003.

Claim 5 is canceled by applicants. [Paper No. 8 filed 5/06/2003].

Claim Objections

Claim 22 remains objected to because of the following informalities:

The claimed list of plant names still contains several typing errors such as repetition of the same plant names (clean copy of amended claim 22, lines 10 and 16-17). Some plant names still have errors, for example: "*Lab lab purpurea*" (clean copy of amended claim 22, line 24).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claim 2 and 26 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 26 as amended remain indefinite with regard to acetic acid concentration "0.1% (v/v)" because it is uncertain whether the claimed concentration is a final concentration in some unidentified system (volume) comprising plant and acetic acid or whether the claimed concentration is a concentration of an original contacting composition/solution which is further diluted in the "aqueous medium", for example. It is uncertain as presently amended whether

"v/v" is intended as a volume of an acetic acid for a volume of plant material or for a volume of some "aqueous medium" including medium for collecting, extracting, exuding and/or macerating.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim rejection under 35 U.S.C. 102(b) as being anticipated by US 5,374,627 [A] has been withdrawn because the method of the cited patent is the one active step method of contacting plant with acetic acid. The cited patent does not clearly disclose the second step of recovering a therapeutically active compound from the plant treated with acetic acid as required by the claimed method as presently amended. Nevertheless, the cited patent US 5,374,627 demonstrates the plant protecting effects of acetic acid or the plant growth promoting effects of acetic acid.

Claims 1-4, 8, 10, 22, 23 and 26 as amended remain rejected under 35 U.S.C. 102(b) as being anticipated by US 5,407,816 [B] as explained in the prior office action and for the reasons below.

Claims are directed to a method for eliciting a compound having therapeutic activity from a plant or plant part wherein the method comprises the step of contacting a living, intact plant or plant part with an effective amount of acetic acid in order to induce production of a compound

having therapeutic activity and recovering or collecting the compound. Some claims are further drawn to the use of particular acetic acid concentration such as 0.1% (v/v) in the method for eliciting a compound having therapeutic activity from a plant or plant part. Some claims are further drawn to the use of water in an aqueous medium, to production of compounds having anti-cancer activity or to providing a library of recovered compounds in the method for eliciting therapeutically active compounds from a plant or plant part. Some claims are further drawn to recovering or collecting the compound by extracting or exuding the compound in an aqueous medium. Some claims are further dawn to the use of plants belonging to the species of *Taxus* including *Taxus media, Taxus baccata* or *Taxus cuspidata.*

US 5,407,816 [B] discloses a method for eliciting compounds having therapeutic activity such as taxol and taxane from plants belonging to the species of *Taxus* including *Taxus media, Taxus baccata* or *Taxus cuspidata* (col. 15, example 6 and table 5 at col. 24) wherein the method comprises the steps of contacting a living plant parts such as plant cell culture or callus culture with an effective amount of acetic acid in form of salt in an aqueous culture medium (table 2), allowing the acetic acid to induce or to improve production of taxol compounds by incubating plant parts or plant cell culture in the aqueous medium and recovering or collecting the compounds exuded in the aqueous medium (col. 15, item 5.2). The cited patent teaches that taxol compounds are characterized by anti-tumor or anti-cancer activity (col. 1, lines 26-30). The cited patent discloses the recovery of several taxol compounds (see tables 8-9) and, thus, it discloses a step of providing a library of recovered therapeutically active compounds. Although the acetic

acid is applied in a form of acetate in the method of the cited patent, however it is reasonably expected that both acetic acid and acetate are effective in the same manner after being ionized in aqueous culture medium which is disclosed by the cited patent and which is required by the claimed method. Moreover, the cited patent clearly teaches that acetate or acetic acid salts are precursors in biosynthesis of therapeutically active compounds such as taxol and taxane, for example: see table 1.b. The cited patent teaches the use of a culture medium with 10 mg/L of sodium acetate (table 2) wherein the use of this particular concentration is effective in obtaining therapeutically active compounds such as taxol and taxane as demonstrated by the method of the cited patent. Although the disclosed amount of acetate or acetic acid in the medium for cell culture of the cited patent is not clearly identical to the claimed amount of "0.1% (v/v)", the claimed method is uncertain with regard to the system wherein the claimed concentration is required. Moreover, it is uncertain as claimed whether the claimed amount "0.1% (v/v)" is a final concentration in a composition/system of the contacting step or whether the amount "0.1% (v/v)" is concentration of some contacting composition/solution which is further dissolved in an aqueous medium of the recovering/collecting step. Thus, the disclosed amount of acetate or acetic acid in the method of the cited patent is considered to be substantially identical to the claimed amount as intended for the present invention particularly in view that the cited method demonstrates a successful production/recovery of therapeutically active compounds taxol and taxanes as the result of application of a medium with acetic acid in amount effective for

production of taxol and taxanes. Therefore, the cited method is considered to anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 7-10, 22, 23 and 26 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,407,816 [B] and US 5,620,875 [C] taken with Staba [U] as explained in the prior office action and for the reasons below.

Claims are directed to a method for eliciting a compound having therapeutic activity from a plant or plant part wherein the method comprises the steps of contacting a living plant or plant part with an effective amount of acetic acid, allowing the acetic acid to induce or to improve production of a compound having therapeutic activity and recovering or collecting the compound. Some claims are further drawn to the use of water in an aqueous medium, to production of compounds having anti-cancer or anti-bacterial activity, to providing a library of recovered compounds in the method for eliciting a compound having therapeutic activity from a plant or plant part. Some claims are further drawn to the use of particular "effective" amount of acetic acid such as "0.1%" in the method for eliciting a compound having therapeutic activity from a plant or plant part. Some claims are further drawn to recovering or collecting the compound by extracting or exuding the compound in an aqueous medium. Some claims are

further dawn to the use of plants belonging to the species of *Taxus* including *Taxus hiksii, Taxus media, Taxus baccata* or *Taxus cuspidata.*

The cited US 5,407,816 [B] is relied upon as explained above for the disclosure a method for producing compounds having therapeutic activity by contacting living plant material with acetic acid or acetic acid derivatives in amounts effective to induce or to improve production of therapeutically active compounds. The cited patent teaches that acetic acid derivatives including acetate (table 1.b) and auxins (table 3) are precursors and regulators of plant-derived therapeutically active compounds such as taxol and taxanes wherein these precursors and regulators allow to induce or to improve plant production of compounds of interest such as taxol and taxanes. In particular, the cited patent teaches that the use of plant parts such as cell culture or plant callus culture in the method for producing therapeutically active compounds but it is lacking disclosure related to the use of other intact parts of living plants comprising roots and/or leaves in a method for eliciting plant derived compounds of interest.

However, US 5,620,875 [C] is relied upon to demonstrate that the same biologically active or therapeutically active compounds such as taxol and taxanes are produced from other parts of plants such as living plant cuttings of *Taxus* which comprise roots and leaves (see abstract) in the culture media comprising acetic acid derivatives or auxins (col. 2, lines 42-43).

The disclosure of both cited patents US 5,407,816 [B] and US 5,620,875 [C] is related to the production of therapeutically active compounds such as taxol and taxanes by plants belonging

to the genus of *Taxus*. But they are lacking disclosure with regard to variety of plants used for obtaining various plant derived compounds.

However, the reference by Staba et al. [U] is relied upon to demonstrate that various plants are used as sources for various therapeutically active compounds including antitumor and antimicrobial compounds (page 237) and that the acetic acid derivatives and/or auxins are important plant growth regulators generally used for plant growth and production (page 7).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to elicit or to produce the same or substantially similar therapeutically active compounds from any part of living plants including plant cell culture or plant cuttings comprising roots and/or leaves with a reasonable expectation of success in obtaining therapeutically active compounds of interest because plant cells from any part of plants are capable to produce the same or similar compounds and they have the same or substantially similar metabolism at least to the extend of production of the same active compounds as demonstrated by methods of both cited patents US 5,407,816 [B] and US 5,620,875 [C] with regard to production of taxol and taxanes. One of skill in the art would have been motivated to use various plants for producing therapeutically active compounds for the expected benefit of providing library of therapeutically active compounds and for the expected benefit of maximizing variety of recovered biologically active compounds as taught and/or suggested by Staba et al. [U]. One of skill in the art would have been motivated to adjust concentrations of culture medium components including concentrations of plant growth regulators and/or plant

biosynthesis precursors such as acetic acid and its derivatives in accordance with the amounts of plant parts or plant materials involved in the production method for the expected benefit of maximizing recovery of biologically active compounds derived from plant or plant parts/materials.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Claims 6 and 24 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,407,816 [B], US 5,620,875 [C] and Staba [U] as applied to claims 1-4, 7-10, 22, 23 and 26 above, and further in view of US 4,871,574 [D] as explained in the prior office action and for the reasons below.

Claims 1-4, 7-10, 22, 23 and 26 as explained above. Claims 6 and 24 are further drawn to the use of extracting/collecting step by macerating plant parts in the method for eliciting therapeutically active compounds.

The references US 5,407,816 [B], US 5,620,875 [C] and Staba [U] are relied upon as explained above. The cited references are silent with regard to macerating step in the method for eliciting therapeutically active compounds.

US 4,871,574 [D] teaches the use of macerating step in the method for eliciting therapeutically active compounds from plant parts. In addition, it also teaches that the use of acetic acid is allowed before or after or during macerating step (see Fig. 1).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to use a macerating step in a method for eliciting therapeutically active compounds from plant parts as taught or suggested by US 4,871,574 [D] with a reasonable expectation of success in obtaining the compounds of interest from plants parts/materials because maceration of plant parts/material is a known technique in the collection or recovery of plant therapeutically active and therapeutically valuable compounds. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Claims 11-21 and 25 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,407,816 [B], US 5,620,875 [C] and Staba [U] as applied to claims 1-4, 7-10, 22, 23 and 26 above, and further in view of Stevens et al. [IDS-C23] and US 3,810,990 [E] as explained in the prior office action and for the reasons below.

Claims 1-4, 7-10, 22, 23 and 26 as explained above. Claims 11-15 and 25 are further drawn to the extracting of therapeutically active compounds from plant leaf cuticular material wherein material comprises wax and wherein the extracting solvents comprise methylene

chloride or chloroform. Claims 17-21 are further drawn to assaying the therapeutically active compounds for antimicrobial activity by determining microbial rates of growth and/or inhibition.

The references US 5,407,816 [B], US 5,620,875 [C] and Staba [U] are relied upon as explained above for the disclosure of methods for eliciting various therapeutically active compounds from various parts of various plants contacted with or grown in the media comprising plant growth regulators and precursors of the therapeutically active compounds including acetic acid derivatives and/or auxins. The cited references US 5,407,816 [B], US 5,620,875 [C] and Staba [U] are lacking disclosure related to recovering therapeutically active compounds from plant leaf cuticular material.

However, the reference by Stevens et al. [IDS-C23] teaches the extracting of therapeutically active flavonoid compounds including quercetin from leaf cuticular material wherein the material is wax and wherein solvents comprise chloroform (abstract and page 805, col. 2, par. 1).

The cited US 3,810,990 [E] is relied upon to demonstrate the antimicrobial activity of flavonoid compounds including quercetin taught in the reference by Stevens et al. [U]. In addition, the cited US 3,810,990 [E] is also relied upon for the disclosure with regard to assaying the therapeutically active compounds/agents including flavonoids for antimicrobial activity by determining microbial rates of growth or inhibiting through the measurements of microbial turbidity and/or counting of microbial colonies in the media/solutions with therapeutically active compounds/agents (see example 7).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to extract therapeutically active compounds from various plant parts or materials including plant leaf cuticular materials with a reasonable expectation of success in obtaining the compounds of interest including antimicrobial compounds because it is has been demonstrated in the prior art that the plant leaf cuticular materials including wax, which is presently claimed, is a known source of biologically active compounds as taught by Stevens et al. [IDS-C23]. One of skill in the art would have been motivated to produce various plant derived therapeutically active compounds including flavonoids of the reference by Stevens et al. [U] by growing plants or plant parts in media comprising plant growth regulators and/or precursors comprising acetic acid derivatives or auxins which are generally used for growing various beneficial plants for the expected results in maximizing production of therapeutically active compounds of interest by various plants as taught and suggested by the cited prior art {US 5,407,816 [B], US 5,620,875 [C], Staba [U]}. The methods for assaying antimicrobial activity of various compounds or agents which are presently claimed are very well known techniques in the field of microbiology as adequately demonstrated by US 3,810,990 [E]. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 5/06/2003 have been fully considered but they are not persuasive.

Main applicants' argument is directed to the idea that the claimed method is drawn to the use of "a living, intact plant or plant part" which is contacted with acetic acid in order to induce production of therapeutically active compounds but the cited prior art is drawn to the use of "a plant cell culture" and/or callus {US 5,407,816} or plant cuttings (US 5,620,875} (see response pages 15-16).

However, the plant cells are the plant parts and the plant cells are the living, intact plant parts which are capable of producing therapeutically active compounds. The instant application does not provide definitions which would exclude plant cell culture, callus or even plant cuttings as disclosed in the as-filed specification and as admitted by applicants (response page 15, par. 2, lines 8-9). Thus, the claimed invention is given a broad interpretation. Therefore, the claimed invention is anticipated by US 5,407,816 as explained above.

Further, with regard to the claim rejection under 35 USC § 103, the cited prior art teaches that elicitors which are used to enhance plant productivity are equally effective in increasing plant metabolite production by both plants and plants cell cultures, for example: see US 5,407,816 at col. 9, line 21. Thus, the argument that the cited prior art fails to suggests contacting a living plant, intact plant does not appear to have persuasive grounds as applied to the claimed invention. Although the plant cell culture methodology of the cited prior art might be different

from the applicants' methodology as argued (response page 16, par. 3), the claimed invention does not require any specific protocols beyond "contacting" plant or plant parts with acetic acid and "recovering"/"collecting" compounds of interest.

With regard to the secondary references applicants appear to argue that the reliance has been misplaced (response page 18, par. 1). However, the secondary references are relied upon to demonstrate that the presently claimed techniques including extracting, exudating, macerating and assaying plant-derived compounds are known prior art techniques commonly applied for collecting and recovering the therapeutically active or valuable plant compounds.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

Art Unit 1651

July 15, 2003.

SANDRA E. SAUCIER
PRIMARY EXAMINER